Clinical trial results:
A Modular Phase I/II, Open-label, Multicentre Study to Assess AZD4573 in Novel Combinations with Anti-cancer Agents in Patients with Advanced Haematological Malignancies

Summary

EudraCT number	2020-001642-18
Trial protocol	IE ES FR IT
Global end of trial date	

Results information

Result version number	v1 (current)
This version publication date	14 May 2025
First version publication date	14 May 2025

Trial information

Trial identification

Sponsor protocol code	D8230C00002

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04630756
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	Södertälje, Södertälje, Sweden, 15185
Public contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com
Scientific contact	Global Clinical Lead, AstraZeneca, +1 877-240-9479, information.center@astrazeneca.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Interim
Date of interim/final analysis	31 December 2024
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 December 2024
Global end of trial reached?	No

Notes:

General information about the trial

Main objective of the trial:

To assess AZD4573 in novel combinations with anti-cancer agents in patients with advanced haematological malignancies.

Protection of trial subjects:

This study was performed in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with ICH/GCP, applicable regulatory requirements and the AstraZeneca policy on Bioethics.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 February 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	30 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 7
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Ireland: 2
Country: Number of subjects enrolled	Korea, Republic of: 5
Country: Number of subjects enrolled	Poland: 3
Country: Number of subjects enrolled	Spain: 1
Country: Number of subjects enrolled	United Kingdom: 1
Country: Number of subjects enrolled	United States: 17
Worldwide total number of subjects	40
EEA total number of subjects	10

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23	0

months)	
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	27
From 65 to 84 years	13
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted from 17 February 2021 to 08 September 2023. Module 1 was conducted at 17 study centers in 10 countries. Module 2 was conducted at 2 sites in the United States.

Pre-assignment

Screening details:

The screening period was 30 days for both parts of the study. Informed Consent Form was signed prior to screening procedures. All study assessments were performed as per the schedule of assessment. Participants who met the eligibility criteria were randomized to study intervention in addition to receiving background local standard of care therapy.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID

Arm description:

Participants received AZD4573 9 mg as Intravenous (IV) infusion once weekly with acalabrutinib 100 mg twice daily.

Arm type	Active comparator
Investigational medicinal product name	AZD4573
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received AZD4573 9 mg as Intravenous (IV) infusion once weekly with acalabrutinib 100 mg twice daily.

Investigational medicinal product name	Acalabrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received AZD4573 9 mg as Intravenous (IV) infusion once weekly with acalabrutinib 100 mg twice daily.

Arm title	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID

Arm description:

Participants received AZD4573 dose expansion to RP2D 12 mg as IV infusion once weekly with acalabrutinib 100 mg twice daily.

Arm type	Active comparator
Investigational medicinal product name	Acalabrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received AZD4573 dose expansion to RP2D 12 mg as IV infusion once weekly with acalabrutinib 100 mg twice daily.

Investigational medicinal product name	AZD4573
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received AZD4573 dose expansion to RP2D 12 mg as IV infusion once weekly with acalabrutinib 100 mg twice daily.

Arm title	Module 2 Period 1 + 2: AZD4573 12 mg monotherapy + combination

Arm description:

Participants received AZD4573 12 mg monotherapy until progression and thereafter received a combination regimen of AZD4573 12 mg once weekly and acalabrutinib 100 mg twice daily.

Arm type	Active comparator
Investigational medicinal product name	Acalabrutinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received AZD4573 12 mg monotherapy until progression and thereafter received a combination regimen of AZD4573 12 mg once weekly and acalabrutinib 100 mg twice daily.

Investigational medicinal product name	AZD4573
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Participants received AZD4573 12 mg monotherapy until progression and thereafter received a combination regimen of AZD4573 12 mg once weekly and acalabrutinib 100 mg twice daily.

Number of subjects in period 1	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID	Module 2 Period 1 + 2: AZD4573 12 mg monotherapy + combination
Started	9	28	3
Completed	8	28	3
Not completed	1	0	0
Ongoing subjects in Post Trial Access Program	1	-	-

Baseline characteristics

Reporting groups	
Reporting group title	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID
Reporting group description:	
Participants received AZD4573 9 mg as Intravenous (IV) infusion once weekly with acalabrutinib 100 mg twice daily.	
Reporting group title	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID
Reporting group description:	
Participants received AZD4573 dose expansion to RP2D 12 mg as IV infusion once weekly with acalabrutinib 100 mg twice daily.	
Reporting group title	Module 2 Period 1 + 2: AZD4573 12 mg monotherapy + combination
Reporting group description:	
Participants received AZD4573 12 mg monotherapy until progression and thereafter received a combination regimen of AZD4573 12 mg once weekly and acalabrutinib 100 mg twice daily.	

Reporting group values	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID	Module 2 Period 1 + 2: AZD4573 12 mg monotherapy + combination
Number of subjects	9	28	3
Age Categorical Units: Participants			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	7	17	3
From 65-84 years	2	11	0
85 years and over	0	0	0
Age Continuous Units: years			
arithmetic mean	51.2	61.7	59.7
standard deviation	± 18.72	± 9.52	± 2.63
Gender Categorical Units: Participants			
Female	4	10	0
Male	5	18	3
Race/Ethnicity Units: Subjects			
Asian	2	8	0
White	6	17	2
Not Reported	1	1	0
Missing	0	2	0
Other	0	0	1

Reporting group values	Total		

Number of subjects	40		
Age Categorical Units: Participants			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	0		
Newborns (0-27 days)	0		
Infants and toddlers (28 days-23 months)	0		
Children (2-11 years)	0		
Adolescents (12-17 years)	0		
Adults (18-64 years)	27		
From 65-84 years	13		
85 years and over	0		
Age Continuous Units: years			
arithmetic mean			
standard deviation	-		
Gender Categorical Units: Participants			
Female	14		
Male	26		
Race/Ethnicity Units: Subjects			
Asian	10		
White	25		
Not Reported	2		
Missing	2		
Other	1		

End points

End points reporting groups

Reporting group title	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID
Reporting group description:	
Participants received AZD4573 9 mg as Intravenous (IV) infusion once weekly with acalabrutinib 100 mg twice daily.	
Reporting group title	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID
Reporting group description:	
Participants received AZD4573 dose expansion to RP2D 12 mg as IV infusion once weekly with acalabrutinib 100 mg twice daily.	
Reporting group title	Module 2 Period 1 + 2: AZD4573 12 mg monotherapy + combination
Reporting group description:	
Participants received AZD4573 12 mg monotherapy until progression and thereafter received a combination regimen of AZD4573 12 mg once weekly and acalabrutinib 100 mg twice daily.	

Primary: Module 1: Number of participants with adverse events

End point title	Module 1: Number of participants with adverse events[1][2]
End point description:	
The safety and tolerability of AZD4573 in combination with acalabrutinib was assessed in the safety analysis set. The safety analysis set included all participants who received any amount of AZD4573 and/or acalabrutinib.	
End point type	Primary
End point timeframe:	
From Screening (Day -30 to Day -1) until disease progression or survival until death (approximately 2.5 years)	

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.

End point values	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	28		
Units: Participants				
Any adverse event (AE)	9	28		
Any serious adverse event (SAE)	4	16		

Statistical analyses

No statistical analyses for this end point

Primary: Module 1: Overall response rate (ORR) of AZD4573 in combination with acalabrutinib

End point title	Module 1: Overall response rate (ORR) of AZD4573 in combination with acalabrutinib[3][4]

End point description:

Objective response rate (ORR), defined as the proportion of participants who have a tumour response (complete response [CR] and partial response [PR]) was assessed in the response evaluable analysis set. The response evaluable analysis set included participants dosed with AZD4573 or acalabrutinib with a baseline tumour assessment.
Here, 999.999 indicates that the value was not calculated due to an insufficient number of participants with events.

End point type	Primary

End point timeframe:

From Screening (Day -30 to Day -1) until disease progression or survival until death (approximately 2.5 years)

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.
[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.

End point values	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	28		
Units: Percentage of participants with response				
number (confidence interval 95%)	44.4 (13.7 to 78.8)	50.0 (30.6 to 69.4)		

Statistical analyses

No statistical analyses for this end point

Primary: Module 2: Number of participants with adverse events

End point title	Module 2: Number of participants with adverse events[5][6]

End point description:

Assessed safety and confirmed the RP2D of AZD4573 monotherapy in MCL participants and assessed the safety and tolerability of AZD4573 in combination with acalabrutinib in participants administered AZD4573 monotherapy in the safety analysis set. The safety analysis set included all participants who received any amount of AZD4573 and/or acalabrutinib.

End point type	Primary

End point timeframe:

From Screening (Day -30 to Day -1) until disease progression or survival until death (approximately 2.5 years)

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.
[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.

End point values	Module 2 Period 1 + 2: AZD4573 12 mg monotherapy + combination			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: Number of Participants				
Any AE	3			
Any SAE	1			

Statistical analyses

No statistical analyses for this end point

Secondary: Module 1: Complete response (CR) rate

End point title	Module 1: Complete response (CR) rate[7]

End point description:

CR, defined as no detectable evidence of tumor, according to the revised response criteria for malignant lymphoma, was assessed in the response evaluable analysis set. The response evaluable analysis set included participants dosed with AZD4573 or acalabrutinib with a baseline tumour assessment.
Here, 999.999 indicates that the value was not calculated due to an insufficient number of participants with events.

End point type	Secondary

End point timeframe:

From Screening (Day -30 to Day -1) until disease progression or survival until death (approximately 2.5 years)

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.

End point values	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	28		
Units: Percentage of participants with response				
number (confidence interval 95%)	11.1 (0.3 to	21.4 (8.3 to		

48.2)	41.0)

Statistical analyses

No statistical analyses for this end point

Secondary: Module 1: Cmax of AZD4573

End point title	Module 1: Cmax of AZD4573[8]

End point description:

Maximum concentration that a drug achieves in a specified compartment or test area of the body after the drug has been administered (Cmax) was measured in the pharmacokinetic analysis set. The pharmacokinetic analysis set included all dosed patients with reportable plasma concentrations and no important adverse events or protocol deviations that may impact PK.
Here, 999.999 indicates that the value was not calculated due to an insufficient number of participants analyzed.

End point type	Secondary

End point timeframe:

Cycle 1 (5 weeks in total) on Day 1 of Week 1, 2 and 3, and Cycle 2 (3 weeks in total) on Day 1 of Week 1

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.

End point values	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	12		
Units: nanograms per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Week 1 Day 1 (n=9, 12)	164.2 (± 469.0)	112.6 (± 70.20)		
Cycle 1 Week 2 Day 1 (n=6, 11)	235.7 (± 359.3)	185.3 (± 50.61)		
Cycle 1 Week 3 Day 1 (n=8, 11)	337.8 (± 194.3)	270.8 (± 38.61)		
Cycle 2 Week 1 Day 1 (n=6, 9)	643.1 (± 578.0)	294.6 (± 48.83)		

Statistical analyses

No statistical analyses for this end point

Secondary: Module 1: Overall survival (OS)

End point title	Module 1: Overall survival (OS)[9]

End point description:

OS, defined as the time from first dose until the date of death from any cause, was measured in the full analysis set. The full analysis set included all participants who received any amount of study intervention.
Here, 999.999 indicates that the value was not calculated due to an insufficient number of participants with events.

End point type	Secondary

End point timeframe:

From Screening (Day -30 to Day -1) until disease progression or survival until death (approximately 2.5 years)

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.

End point values	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	28		
Units: Months				
median (confidence interval 95%)	999.999 (3.52 to 999.999)	8.8 (3.91 to 999.999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Module 1: Duration of response (DoR)

End point title	Module 1: Duration of response (DoR)[10]

End point description:

DoR, defined as the time from the first objective response of CR or PR to the time of documented disease progression or death due to any cause, whichever occurs first, was measured in the response evaluable analysis set. The response evaluable analysis set included participants dosed with AZD4573 or acalabrutinib with a baseline tumour assessment.
Here, 999.999 indicates that the value was not calculated due to an insufficient number of participants with events.

End point type	Secondary

End point timeframe:

From Screening (Day -30 to Day -1) until disease progression or survival until death (approximately 2.5 years)

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.

End point values	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	28		
Units: Months				
median (confidence interval 95%)	4.4 (4.1 to 999.999)	3.3 (1.2 to 6.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Module 1: Progression free survival (PFS)

End point title	Module 1: Progression free survival (PFS)[11]

End point description:

PFS, defined as the time from first dose date to documented disease progression, or death from any cause, whichever occurs first, was measured in the full analysis set. The full analysis set included all participants who received any amount of study intervention.
Here, 999.999 indicates that the value was not calculated due to an insufficient number of participants with events.

End point type	Secondary

End point timeframe:

From Screening (Day -30 to Day -1) until disease progression or survival until death (approximately 2.5 years)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.

End point values	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	28		
Units: Months				
median (confidence interval 95%)	2.1 (0.30 to 6.44)	2.8 (1.91 to 3.98)		

Statistical analyses

No statistical analyses for this end point

Secondary: Module 1: Cmax of acalabrutinib

End point title	Module 1: Cmax of acalabrutinib[12]

End point description:

Maximum concentration that a drug achieves in a specified compartment or test area of the body after the drug has been administered (Cmax) was measured in the pharmacokinetic analysis set. The pharmacokinetic analysis set included all dosed patients with reportable plasma concentrations and no important adverse events or protocol deviations that may impact PK.
Here, 999.999 indicates that the value was not calculated due to an insufficient number of participants analyzed.

End point type	Secondary

End point timeframe:

Cycle 1 (5 weeks in total) on Day 1 of Week 1, 2 and 3, and Cycle 2 (3 weeks in total) on Day 1 of Week 1

Notes:

[12] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.

End point values	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	12		
Units: nanograms per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Week 1 Day 1 (n=6, 11)	219.9 (± 66.94)	306.1 (± 76.06)		
Cycle 1 Week 2 Day 1 (n=6, 10)	209.8 (± 45.79)	322.7 (± 95.53)		
Cycle 1 Week 3 Day 1 (n=7, 10)	232.1 (± 74.77)	274.2 (± 78.98)		
Cycle 2 Week 1 Day 1 (n=5, 8)	217.5 (± 100.8)	256.7 (± 67.75)		

Statistical analyses

No statistical analyses for this end point

Secondary: Module 1: Cmax of ACP-5862

End point title	Module 1: Cmax of ACP-5862[13]

End point description:

Maximum concentration that a drug achieves in a specified compartment or test area of the body after the drug has been administered (Cmax) was measured in the pharmacokinetic analysis set. The pharmacokinetic analysis set included all dosed patients with reportable plasma concentrations and no important adverse events or protocol deviations that may impact PK.
Here, 999.999 indicates that the value was not calculated due to an insufficient number of participants analyzed.

End point type	Secondary

End point timeframe:

Cycle 1 (5 weeks in total) on Day 1 of Week 1, 2 and 3, and Cycle 2 (3 weeks in total) on Day 1 of Week 1

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.

End point values	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	11		
Units: nanograms per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Week 1 Day 1 (n=6, 11)	199.2 (± 129.3)	250.2 (± 78.12)		
Cycle 1 Week 2 Day 1 (n=6, 10)	382.1 (± 51.58)	288.0 (± 63.26)		
Cycle 1 Week 3 Day 1 (n=7, 10)	320.8 (± 35.92)	282.9 (± 55.76)		
Cycle 2 Week 1 Day 1 (n=5, 8)	304.6 (± 79.28)	251.8 (± 45.54)		

Statistical analyses

No statistical analyses for this end point

Secondary: Module 1: AUClast of acalabrutinib

End point title	Module 1: AUClast of acalabrutinib[14]

End point description:

The area under the plasma concentration time curve from zero to the time of the last measurable concentration (AUClast) was measured in the pharmacokinetic analysis set. The pharmacokinetic analysis set included all dosed patients with reportable plasma concentrations and no important adverse events or protocol deviations that may impact PK.
Here, 999.999 indicates that the value was not calculated due to an insufficient number of participants analyzed.

End point type	Secondary

End point timeframe:

Cycle 1 (5 weeks in total) on Day 1 of Week 1, 2 and 3, and Cycle 2 (3 weeks in total) on Day 1 of Week 1

Notes:

[14] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.

End point values	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	11		
Units: time*nanogram per milliliter (h*ng/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Week 1 Day 1 (n=6, 11)	493.9 (± 58.91)	631.4 (± 69.98)		
Cycle 1 Week 2 Day 1 (n=6, 10)	520.9 (± 46.04)	638.2 (± 81.66)		
Cycle 1 Week 3 Day 1 (n=7, 10)	475.9 (± 45.57)	570.7 (± 67.75)		
Cycle 2 Week 1 Day 1 (n=5, 8)	481.8 (± 58.39)	424.5 (± 162.8)		

Statistical analyses

No statistical analyses for this end point

Secondary: Module 1: AUClast of AZD4573

End point title	Module 1: AUClast of AZD4573[15]

End point description:

The area under the plasma concentration time curve from zero to the time of the last measurable concentration (AUClast) was measured in the pharmacokinetic analysis set. The pharmacokinetic analysis set included all dosed patients with reportable plasma concentrations and no important adverse events or protocol deviations that may impact PK.
Here, 999.999 indicates that the value was not calculated due to an insufficient number of participants analyzed.

End point type	Secondary

End point timeframe:

Cycle 1 (5 weeks in total) on Day 1 of Week 1, 2 and 3, and Cycle 2 (3 weeks in total) on Day 1 of Week 1

Notes:

[15] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.

End point values	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	12		
Units: time*nanogram per milliliter (h*ng/mL)				
geometric mean (geometric coefficient of variation)				

Cycle 1 Week 1 Day 1 (n=6, 12)	532.9 (± 164.5)	561.3 (± 60.83)		
Cycle 1 Week 2 Day 1 (n=6, 11)	845.3 (± 134.8)	929.0 (± 55.85)		
Cycle 1 Week 3 Day 1 (n=8, 11)	1273 (± 127.7)	1697 (± 62.55)		
Cycle 2 Week 1 Day 1 (n=6, 9)	1939 (± 330.9)	1439 (± 90.63)		

Statistical analyses

No statistical analyses for this end point

Secondary: Module 1: AUClast of ACP-5862

End point title	Module 1: AUClast of ACP-5862[16]

End point description:

The area under the plasma concentration time curve from zero to the time of the last measurable concentration (AUClast) was measured in the pharmacokinetic analysis set. The pharmacokinetic analysis set included all dosed patients with reportable plasma concentrations and no important adverse events or protocol deviations that may impact PK.
Here, 999.999 indicates that the value was not calculated due to an insufficient number of participants analyzed.

End point type	Secondary

End point timeframe:

Cycle 1 (5 weeks in total) on Day 1 of Week 1, 2 and 3, and Cycle 2 (3 weeks in total) on Day 1 of Week 1

Notes:

[16] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.

End point values	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	11		
Units: time*nanogram per milliliter (h*ng/mL)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Week 1 Day 1 (n=6, 11)	673.9 (± 93.89)	870.8 (± 68.73)		
Cycle 1 Week 2 Day 1 (n=6, 10)	1173 (± 48.03)	1135 (± 54.95)		
Cycle 1 Week 3 Day 1 (n=7, 10)	1204 (± 36.24)	1093 (± 54.50)		
Cycle 2 Week 1 Day 1 (n=5, 8)	941.9 (± 102.5)	849.3 (± 60.56)		

Statistical analyses

No statistical analyses for this end point

Secondary: Module 1: AUCinf of AZD4573

End point title	Module 1: AUCinf of AZD4573[17]

End point description:

The area under the plasma concentration time curve from zero extrapolated to infinity (AUCinf) was measured in the pharmacokinetic analysis set. The pharmacokinetic analysis set included all dosed patients with reportable plasma concentrations and no important adverse events or protocol deviations that may impact PK.
Here, 999.999 indicates that the value was not calculated due to an insufficient number of participants analyzed.

End point type	Secondary

End point timeframe:

Cycle 1 (5 weeks in total) on Day 1 of Week 1, 2 and 3, and Cycle 2 (3 weeks in total) on Day 1 of Week 1

Notes:

[17] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.

End point values	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	9		
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Week 1 Day 1 (n=1, 4)	999.999 (± 999.999)	640.5 (± 15.33)		
Cycle 1 Week 2 Day 1 (n=4, 6)	1188 (± 160.1)	847.4 (± 68.22)		
Cycle 1 Week 3 Day 1 (n=5, 9)	1588 (± 169.6)	1736 (± 67.09)		
Cycle 2 Week 1 Day 1 (n=4, 5)	4672 (± 162.9)	1853 (± 29.55)		

Statistical analyses

No statistical analyses for this end point

Secondary: Module 1: AUCinf of acalabrutinib

End point title	Module 1: AUCinf of acalabrutinib[18]

End point description:

The area under the plasma concentration time curve from zero extrapolated to infinity (AUCinf) was measured in the pharmacokinetic analysis set. The pharmacokinetic analysis set included all dosed patients with reportable plasma concentrations and no important adverse events or protocol deviations that may impact PK.
Here, 999.999 indicates that the value was not calculated due to an insufficient number of participants analyzed.

End point type	Secondary

End point timeframe:

Cycle 1 (5 weeks in total) on Day 1 of Week 1, 2 and 3, and Cycle 2 (3 weeks in total) on Day 1 of Week 1

Notes:

[18] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.

End point values	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3	5		
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Week 1 Day 1 (n=3, 5)	600.1 (± 34.99)	501.3 (± 58.03)		
Cycle 1 Week 2 Day 1 (n=0, 0)	999.999 (± 999.999)	999.999 (± 999.999)		
Cycle 1 Week 3 Day 1 (n=0, 0)	999.999 (± 999.999)	999.999 (± 999.999)		
Cycle 2 Week 1 Day 1 (n=0, 0)	999.999 (± 999.999)	999.999 (± 999.999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Module 1: AUCinf of ACP-5862

End point title	Module 1: AUCinf of ACP-5862[19]

End point description:

The area under the plasma concentration time curve from zero extrapolated to infinity (AUCinf) was measured in the pharmacokinetic analysis set. The pharmacokinetic analysis set included all dosed patients with reportable plasma concentrations and no important adverse events or protocol deviations that may impact PK.
Here, 999.999 indicates that the value was not calculated due to an insufficient number of participants analyzed.

End point type	Secondary

End point timeframe:

Cycle 1 (5 weeks in total) on Day 1 of Week 1, 2 and 3, and Cycle 2 (3 weeks in total) on Day 1 of Week 1

Notes:

[19] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.

End point values	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2	4		
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)				
Cycle 1 Week 1 Day 1 (n=2, 4)	999.999 (± 999.999)	935.2 (± 38.81)		
Cycle 1 Week 2 Day 1 (n=0, 0)	999.999 (± 999.999)	999.999 (± 999.999)		
Cycle 1 Week 3 Day 1 (n=0, 0)	999.999 (± 999.999)	999.999 (± 999.999)		
Cycle 2 Week 1 Day 1 (n=0, 0)	999.999 (± 999.999)	999.999 (± 999.999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Module 1: tmax of AZD4573

End point title	Module 1: tmax of AZD4573[20]

End point description:

The time to reach peak or maximum observed concentration following drug administration (tmax) was measured in the pharmacokinetic analysis set. The pharmacokinetic analysis set included all dosed patients with reportable plasma concentrations and no important adverse events or protocol deviations that may impact PK.

End point type	Secondary

End point timeframe:

Cycle 1 (5 weeks in total) on Day 1 of Week 1, 2 and 3, and Cycle 2 (3 weeks in total) on Day 1 of Week 1

Notes:

[20] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.

End point values	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	12		
Units: Hours (h)				
median (full range (min-max))				
Cycle 1 Week 1 Day 1 (n=6, 12)	1.992 (0.750 to 4.17)	2.083 (1.00 to 10.5)		
Cycle 1 Week 2 Day 1 (n=6, 11)	1.892 (1.00 to 3.00)	2.033 (1.05 to 2.15)		
Cycle 1 Week 3 Day 1 (n=8, 11)	2.192 (0.933 to 3.32)	2.000 (1.03 to 2.15)		

Cycle 2 Week 1 Day 1 (n=6, 9)	2.067 (1.00 to 2.22)	2.083 (1.85 to 3.63)		

Statistical analyses

No statistical analyses for this end point

Secondary: Module 1: tmax of acalabrutinib

End point title	Module 1: tmax of acalabrutinib[21]

End point description:

The time to reach peak or maximum observed concentration following drug administration (tmax) was measured in the pharmacokinetic analysis set. The pharmacokinetic analysis set included all dosed patients with reportable plasma concentrations and no important adverse events or protocol deviations that may impact PK.
Here, 999.999 indicates that the value was not calculated due to an insufficient number of participants analyzed.

End point type	Secondary

End point timeframe:

Cycle 1 (5 weeks in total) on Day 1 of Week 1, 2 and 3, and Cycle 2 (3 weeks in total) on Day 1 of Week 1

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.

End point values	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	11		
Units: Hours (h)				
median (full range (min-max))				
Cycle 1 Week 1 Day 1 (n=6, 11)	1.242 (1.02 to 3.80)	1.117 (0.933 to 2.65)		
Cycle 1 Week 2 Day 1 (n=6, 9)	2.017 (1.00 to 4.52)	1.133 (0.950 to 11.6)		
Cycle 1 Week 3 Day 1 (n=7, 10)	1.233 (1.00 to 3.17)	1.433 (0.850 to 4.00)		
Cycle 2 Week 1 Day 1 (n=5, 7)	1.933 (1.03 to 5.75)	1.200 (0.833 to 2.25)		

Statistical analyses

No statistical analyses for this end point

Secondary: Module 1: tmax of ACP-5862

End point title	Module 1: tmax of ACP-5862[22]

End point description:

The time to reach peak or maximum observed concentration following drug administration (tmax) was measured in the pharmacokinetic analysis set. The pharmacokinetic analysis set included all dosed patients with reportable plasma concentrations and no important adverse events or protocol deviations that may impact PK.
Here, 999.999 indicates that the value was not calculated due to an insufficient number of participants analyzed.

End point type	Secondary

End point timeframe:

Cycle 1 (5 weeks in total) on Day 1 of Week 1, 2 and 3, and Cycle 2 (3 weeks in total) on Day 1 of Week 1

Notes:

[22] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.

End point values	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	7	11		
Units: Hours (h)				
median (full range (min-max))				
Cycle 1 Week 1 Day 1 (n=6, 11)	3.067 (1.02 to 7.00)	1.117 (0.933 to 7.08)		
Cycle 1 Week 2 Day 1 (n=6, 9)	2.075 (1.08 to 7.52)	2.117 (1.05 to 11.6)		
Cycle 1 Week 3 Day 1 (n=7, 10)	1.233 (1.00 to 4.58)	1.892 (0.850 to 4.00)		
Cycle 2 Week 1 Day 1 (n=5, 7)	2.167 (2.05 to 8.92)	2.117 (0.917 to 4.13)		

Statistical analyses

No statistical analyses for this end point

Secondary: Module 1: t1/2 of AZD4573

End point title	Module 1: t1/2 of AZD4573[23]

End point description:

The time taken for half the initial dose of drug administered to be eliminated from the body (t1/2) was measured in the pharmacokinetic analysis set. The pharmacokinetic analysis set included all dosed patients with reportable plasma concentrations and no important adverse events or protocol deviations that may impact PK.
Here, 999.999 indicates that the value was not calculated due to an insufficient number of participants analyzed.

End point type	Secondary

End point timeframe:

Cycle 1 (5 weeks in total) on Day 1 of Week 1, 2 and 3, and Cycle 2 (3 weeks in total) on Day 1 of Week 1

Notes:

[23] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.

End point values	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	10		
Units: Hours (h)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Week 1 Day 1 (n=1, 5)	999.999 (± 999.999)	3.692 (± 37.98)		
Cycle 1 Week 2 Day 1 (n=4, 7)	3.364 (± 43.80)	5.407 (± 73.47)		
Cycle 1 Week 3 Day 1 (n=5, 10)	4.465 (± 42.28)	6.177 (± 30.16)		
Cycle 2 Week 1 Day 1 (n=4, 5)	6.508 (± 30.61)	5.808 (± 25.52)		

Statistical analyses

No statistical analyses for this end point

Secondary: Module 1: t1/2 of acalabrutinib

End point title	Module 1: t1/2 of acalabrutinib[24]

End point description:

The time taken for half the initial dose of drug administered to be eliminated from the body (t1/2) was measured in the pharmacokinetic analysis set. The pharmacokinetic analysis set included all dosed patients with reportable plasma concentrations and no important adverse events or protocol deviations that may impact PK.
Here, 999.999 indicates that the value was not calculated due to an insufficient number of participants analyzed.

End point type	Secondary

End point timeframe:

Cycle 1 (5 weeks in total) on Day 1 of Week 1, 2 and 3, and Cycle 2 (3 weeks in total) on Day 1 of Week 1

Notes:

[24] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.

End point values	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6	6		
Units: Hours (h)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Week 1 Day 1 (n=3, 5)	1.332 (± 22.01)	1.108 (± 12.06)		
Cycle 1 Week 2 Day 1 (n=3, 6)	1.383 (± 49.15)	1.274 (± 25.09)		
Cycle 1 Week 3 Day 1 (n=6, 6)	1.238 (± 20.93)	1.546 (± 38.08)		
Cycle 2 Week 1 Day 1 (n=2, 4)	999.999 (± 999.999)	1.398 (± 32.20)		

Statistical analyses

No statistical analyses for this end point

Secondary: Module 1: t1/2 of ACP-5862

End point title	Module 1: t1/2 of ACP-5862[25]

End point description:

The time taken for half the initial dose of drug administered to be eliminated from the body (t1/2) was measured in the pharmacokinetic analysis set. The pharmacokinetic analysis set included all dosed patients with reportable plasma concentrations and no important adverse events or protocol deviations that may impact PK.
Here, 999.999 indicates that the value was not calculated due to an insufficient number of participants analyzed.

End point type	Secondary

End point timeframe:

Cycle 1 (5 weeks in total) on Day 1 of Week 1, 2 and 3, and Cycle 2 (3 weeks in total) on Day 1 of Week 1

Notes:

[25] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: The endpoint title is specific to the arms which are presented only. Participants in Module 2: Periods 1 and 2 were not assessed for this outcome measure. Hence, only the arms which are referenced in the title are presented per outcome measure.

End point values	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5	6		
Units: Hours (h)				
geometric mean (geometric coefficient of variation)				
Cycle 1 Week 1 Day 1 (n=2, 5)	999.999 (± 999.999)	2.568 (± 33.27)		

Cycle 1 Week 2 Day 1 (n=2, 4)	999.999 (± 999.999)	3.021 (± 47.65)		
Cycle 1 Week 3 Day 1 (n=5, 6)	2.650 (± 34.68)	3.557 (± 38.06)		
Cycle 2 Week 1 Day 1 (n=0, 2)	999.999 (± 999.999)	999.999 (± 999.999)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From Screening (Day -30 to Day -1) until disease progression or survival until death (approximately 2.5 years)	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	26.0

Reporting groups	
Reporting group title	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID
Reporting group description:	
Participants received AZD4573 9 mg as Intravenous (IV) infusion once weekly with acalabrutinib 100 mg twice daily.	
Reporting group title	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID
Reporting group description:	
Participants received AZD4573 dose expansion to RP2D 12 mg as IV infusion once weekly with acalabrutinib 100 mg twice daily.	
Reporting group title	Module 2 Period 1 + 2: AZD4573 12 mg monotherapy + combination
Reporting group description:	
Participants received AZD4573 12 mg monotherapy until progression and thereafter received a combination regimen of AZD4573 12 mg once weekly and acalabrutinib 100 mg twice daily.	

Serious adverse events	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID	Module 2 Period 1 + 2: AZD4573 12 mg monotherapy + combination
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 9 (44.44%)	16 / 28 (57.14%)	2 / 3 (66.67%)
number of deaths (all causes)	4	16	0
number of deaths resulting from adverse events	0	2	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic neoplasm			
subjects affected / exposed	0 / 9 (0.00%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	0 / 9 (0.00%)	2 / 28 (7.14%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic enzyme increased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test abnormal			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Presyncope			
subjects affected / exposed	0 / 9 (0.00%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 9 (0.00%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Seizure			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 9 (0.00%)	2 / 28 (7.14%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypogammaglobulinaemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	0 / 9 (0.00%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			

subjects affected / exposed	0 / 9 (0.00%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Cellulitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device related infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 9 (0.00%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia adenoviral			
alternative dictionary used: MedDRA v26.0			
subjects affected / exposed	0 / 9 (0.00%)	4 / 28 (14.29%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis B reactivation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 28 (0.00%)	1 / 3 (33.33%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 virus test			
subjects affected / exposed	0 / 9 (0.00%)	2 / 28 (7.14%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Module 1 Part A: AZD4573 9 mg + 100g acalabrutinib BID	Module 1 Part B: AZD4573 12 mg + 100g acalabrutinib BID	Module 2 Period 1 + 2: AZD4573 12 mg monotherapy + combination
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)	28 / 28 (100.00%)	3 / 3 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lip neoplasm benign			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Orthostatic hypotension			
subjects affected / exposed	1 / 9 (11.11%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Hypotension			
subjects affected / exposed	0 / 9 (0.00%)	4 / 28 (14.29%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Deep vein thrombosis			
subjects affected / exposed	0 / 9 (0.00%)	2 / 28 (7.14%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
General disorders and administration site conditions			
Chest discomfort			
subjects affected / exposed	0 / 9 (0.00%)	0 / 28 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 9 (0.00%)	6 / 28 (21.43%)	2 / 3 (66.67%)
occurrences (all)	0	6	2
Peripheral swelling			
subjects affected / exposed	0 / 9 (0.00%)	2 / 28 (7.14%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Oedema peripheral			

subjects affected / exposed	3 / 9 (33.33%)	2 / 28 (7.14%)	0 / 3 (0.00%)
occurrences (all)	3	2	0
Injection site erythema			
subjects affected / exposed	1 / 9 (11.11%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Fatigue			
subjects affected / exposed	2 / 9 (22.22%)	11 / 28 (39.29%)	2 / 3 (66.67%)
occurrences (all)	3	12	2
Device related thrombosis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Catheter site related reaction			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Catheter site erythema			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Asthenia			
subjects affected / exposed	1 / 9 (11.11%)	2 / 28 (7.14%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Application site erosion			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Hypoxia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 28 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Rhinorrhea			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Oropharyngeal pain			
subjects affected / exposed	2 / 9 (22.22%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Nasal congestion			

subjects affected / exposed	0 / 9 (0.00%)	3 / 28 (10.71%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Hiccups			
subjects affected / exposed	1 / 9 (11.11%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Epistaxis			
subjects affected / exposed	0 / 9 (0.00%)	2 / 28 (7.14%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Dyspnoea			
subjects affected / exposed	0 / 9 (0.00%)	5 / 28 (17.86%)	2 / 3 (66.67%)
occurrences (all)	0	5	2
Cough			
subjects affected / exposed	1 / 9 (11.11%)	4 / 28 (14.29%)	1 / 3 (33.33%)
occurrences (all)	2	6	1
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 9 (11.11%)	3 / 28 (10.71%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 9 (33.33%)	15 / 28 (53.57%)	0 / 3 (0.00%)
occurrences (all)	12	55	0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood bilirubin increased			
subjects affected / exposed	1 / 9 (11.11%)	3 / 28 (10.71%)	0 / 3 (0.00%)
occurrences (all)	1	5	0
Alanine aminotransferase increased			
subjects affected / exposed	3 / 9 (33.33%)	15 / 28 (53.57%)	0 / 3 (0.00%)
occurrences (all)	6	46	0
Amylase increased			
subjects affected / exposed	0 / 9 (0.00%)	2 / 28 (7.14%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Transaminases increased			

subjects affected / exposed	1 / 9 (11.11%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Weight increased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Lipase increased			
subjects affected / exposed	1 / 9 (11.11%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Blood creatinine increased			
subjects affected / exposed	1 / 9 (11.11%)	4 / 28 (14.29%)	1 / 3 (33.33%)
occurrences (all)	1	5	2
Fibrin D dimer increased			
subjects affected / exposed	1 / 9 (11.11%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	2 / 9 (22.22%)	3 / 28 (10.71%)	0 / 3 (0.00%)
occurrences (all)	3	6	0
White blood cell count decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 28 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Hepatic enzyme increased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Glutamate dehydrogenase increased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 9 (11.11%)	5 / 28 (17.86%)	0 / 3 (0.00%)
occurrences (all)	2	6	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 9 (0.00%)	2 / 28 (7.14%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Atrial fibrillation			

subjects affected / exposed	0 / 9 (0.00%)	2 / 28 (7.14%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 9 (11.11%)	5 / 28 (17.86%)	0 / 3 (0.00%)
occurrences (all)	1	7	0
Dizziness postural			
subjects affected / exposed	1 / 9 (11.11%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Headache			
subjects affected / exposed	1 / 9 (11.11%)	6 / 28 (21.43%)	1 / 3 (33.33%)
occurrences (all)	1	8	1
Peripheral sensory neuropathy			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	2	0	0
Presyncope			
subjects affected / exposed	0 / 9 (0.00%)	3 / 28 (10.71%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Blood and lymphatic system disorders			
Thrombocytopenia			
subjects affected / exposed	6 / 9 (66.67%)	16 / 28 (57.14%)	1 / 3 (33.33%)
occurrences (all)	11	46	3
Neutropenia			
subjects affected / exposed	9 / 9 (100.00%)	25 / 28 (89.29%)	3 / 3 (100.00%)
occurrences (all)	86	126	6
Lymphopenia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Leukopenia			
subjects affected / exposed	3 / 9 (33.33%)	2 / 28 (7.14%)	0 / 3 (0.00%)
occurrences (all)	3	2	0
Anaemia			
subjects affected / exposed	3 / 9 (33.33%)	14 / 28 (50.00%)	1 / 3 (33.33%)
occurrences (all)	3	23	1
Ear and labyrinth disorders			

Deafness			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Punctate keratitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Scintillating scotoma			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 9 (22.22%)	2 / 28 (7.14%)	2 / 3 (66.67%)
occurrences (all)	2	2	2
Abdominal distension			
subjects affected / exposed	1 / 9 (11.11%)	1 / 28 (3.57%)	1 / 3 (33.33%)
occurrences (all)	1	1	1
Abdominal discomfort			
subjects affected / exposed	1 / 9 (11.11%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Abdominal pain upper			
subjects affected / exposed	1 / 9 (11.11%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Dry mouth			
subjects affected / exposed	0 / 9 (0.00%)	0 / 28 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Abdominal pain lower			
subjects affected / exposed	0 / 9 (0.00%)	0 / 28 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Vomiting			
subjects affected / exposed	1 / 9 (11.11%)	11 / 28 (39.29%)	1 / 3 (33.33%)
occurrences (all)	1	19	1
Saliva altered			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nausea			

subjects affected / exposed	4 / 9 (44.44%)	19 / 28 (67.86%)	2 / 3 (66.67%)
occurrences (all)	7	33	2
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 9 (0.00%)	4 / 28 (14.29%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Epigastric discomfort			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Dysphagia			
subjects affected / exposed	0 / 9 (0.00%)	2 / 28 (7.14%)	1 / 3 (33.33%)
occurrences (all)	0	3	1
Dyspepsia			
subjects affected / exposed	1 / 9 (11.11%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Diarrhoea			
subjects affected / exposed	3 / 9 (33.33%)	14 / 28 (50.00%)	3 / 3 (100.00%)
occurrences (all)	7	32	5
Constipation			
subjects affected / exposed	0 / 9 (0.00%)	4 / 28 (14.29%)	2 / 3 (66.67%)
occurrences (all)	0	4	2
Hepatobiliary disorders			
Hyperbilirubinaemia			
subjects affected / exposed	0 / 9 (0.00%)	3 / 28 (10.71%)	0 / 3 (0.00%)
occurrences (all)	0	9	0
Skin and subcutaneous tissue disorders			
Rash macular			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Night sweats			
subjects affected / exposed	0 / 9 (0.00%)	3 / 28 (10.71%)	1 / 3 (33.33%)
occurrences (all)	0	4	1
Keratosis pilaris			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Petechiae			

subjects affected / exposed	0 / 9 (0.00%)	0 / 28 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Rash maculo-papular			
subjects affected / exposed	2 / 9 (22.22%)	2 / 28 (7.14%)	0 / 3 (0.00%)
occurrences (all)	3	2	0
Renal and urinary disorders			
Glycosuria			
subjects affected / exposed	1 / 9 (11.11%)	2 / 28 (7.14%)	0 / 3 (0.00%)
occurrences (all)	1	3	0
Proteinuria			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Bone pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 28 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	0 / 9 (0.00%)	0 / 28 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Myalgia			
subjects affected / exposed	2 / 9 (22.22%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences (all)	2	1	0
Muscle spasms			
subjects affected / exposed	0 / 9 (0.00%)	3 / 28 (10.71%)	0 / 3 (0.00%)
occurrences (all)	0	3	0
Back pain			
subjects affected / exposed	1 / 9 (11.11%)	5 / 28 (17.86%)	1 / 3 (33.33%)
occurrences (all)	1	5	1
Arthralgia			
subjects affected / exposed	1 / 9 (11.11%)	2 / 28 (7.14%)	0 / 3 (0.00%)
occurrences (all)	2	3	0
Infections and infestations			
COVID-19			
subjects affected / exposed	3 / 9 (33.33%)	2 / 28 (7.14%)	0 / 3 (0.00%)
occurrences (all)	4	2	0
Cellulitis			

subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Escherichia urinary tract infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	1 / 3 (33.33%)
occurrences (all)	1	0	1
Fungal skin infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 9 (0.00%)	2 / 28 (7.14%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Oral candidiasis			
subjects affected / exposed	0 / 9 (0.00%)	2 / 28 (7.14%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Oral herpes			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pharyngitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	1 / 9 (11.11%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Respiratory syncytial virus infection			
subjects affected / exposed	0 / 9 (0.00%)	2 / 28 (7.14%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Rhinovirus infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Diverticulitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 28 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Catheter site infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 28 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			

Decreased appetite			
subjects affected / exposed	1 / 9 (11.11%)	4 / 28 (14.29%)	1 / 3 (33.33%)
occurrences (all)	1	4	1
Dehydration			
subjects affected / exposed	1 / 9 (11.11%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences (all)	1	1	0
Hyperglycaemia			
subjects affected / exposed	0 / 9 (0.00%)	3 / 28 (10.71%)	0 / 3 (0.00%)
occurrences (all)	0	4	0
Hyperkalaemia			
subjects affected / exposed	1 / 9 (11.11%)	2 / 28 (7.14%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Hyperphosphataemia			
subjects affected / exposed	0 / 9 (0.00%)	8 / 28 (28.57%)	2 / 3 (66.67%)
occurrences (all)	0	9	3
Hypertriglyceridaemia			
subjects affected / exposed	1 / 9 (11.11%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences (all)	4	4	0
Hypoalbuminaemia			
subjects affected / exposed	0 / 9 (0.00%)	2 / 28 (7.14%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Hypocalcaemia			
subjects affected / exposed	0 / 9 (0.00%)	4 / 28 (14.29%)	0 / 3 (0.00%)
occurrences (all)	0	7	0
Hypokalaemia			
subjects affected / exposed	0 / 9 (0.00%)	8 / 28 (28.57%)	0 / 3 (0.00%)
occurrences (all)	0	14	0
Hypomagnesaemia			
subjects affected / exposed	0 / 9 (0.00%)	2 / 28 (7.14%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Hyponatraemia			
subjects affected / exposed	1 / 9 (11.11%)	1 / 28 (3.57%)	0 / 3 (0.00%)
occurrences (all)	1	2	0
Hypophosphataemia			
subjects affected / exposed	0 / 9 (0.00%)	7 / 28 (25.00%)	0 / 3 (0.00%)
occurrences (all)	0	14	0

Tumour lysis syndrome subjects affected / exposed occurrences (all)	0 / 9 (0.00%) 0	6 / 28 (21.43%) 13	0 / 3 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 July 2020	Amended core inclusion criteria to update calculated creatinine clearance from ≥ 50 mL/minute to ≥ 60 mL/minute, specify that participants should be able to swallow capsules and remove serum creatinine from criteria for adequate organ function; updated exclusion criteria regarding anticoagulant therapy; updated justification for dose; updated exclusion criteria regarding participants on anticoagulant therapy; updated DLT criteria for timing, febrile neutropenia and thrombocytopenia, and definition of isolated changes in GGT in DLT criteria exclusions; included warfarin or equivalent vitamin K antagonists to prohibited concomitant therapies; added requirement that acalabrutinib treatment must be discontinued if participants require vitamin K antagonist or combined administration of antiplatelet and therapeutic anticoagulation while on study; added additional safety monitoring and potential stopping criteria.
21 July 2021	Updated study design to include additional Module 2 AZD4573 monotherapy window followed by combination therapy with acalabrutinib; updated requirements for overnight hospitalization based on emerging data from ongoing FTIH study; updated exploratory objectives; amended Module 1 description to include MZL participants; changed data cut-off for primary analysis for each expansion subgroup from after all participants have had the opportunity to be followed for at least 12 months to at least 6 months; added clarification on TLS monitoring, updated study synopsis to reflect additional module and addition of participants with r/r MZL to Module 1.
01 August 2022	Updated core exclusion criteria: reduced CAR-T criteria to within 60 days prior to first dose of study drug; updated Module 1 part B: changed so that any safe dose level can be backfilled to approximately 21 patients instead of 12; removed Module 1 exclusion criteria for BTK inhibitors; updated schedule of activities to have less frequent assessments in earlier cycles; updated PHL process to reflect experience of AZD4573 liver safety profile.
01 June 2023	Updated overall study design to include rationale as to why study has permanently halted; added text throughout protocol to define that participants still receiving clinical benefit of treatment may continue to receive study treatment, initially planned interim analysis will not be performed, and Module 1 DLBCL cohorts will be pooled for the purpose of primary analysis; updated end of study definition in core section of the protocol.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Due to the overall AZD4573 development programme being discontinued as part of a strategic portfolio decision, available data analyzed for this study is limited.

Notes: